Clinical Criteria for Hepatitis C (HCV) Therapy

Diagnosis

- Must have chronic hepatitis C (HCV infection > 6 months), genotype and sub-genotype specified to determine the length of therapy;
- Liver biopsy or other accepted test demonstrating liver fibrosis corresponding to Metavir score of greater than or equal to 2;
- Consult performed and medication prescribed by a provider specializing in infectious disease, gastroenterology, hepatology or Hepatitis C.

Patient Treatment Plan

- Patient must have a treatment plan developed by the specialist.
- If patient or their partner is of childbearing age, she must utilize 2 forms of contraception if a ribavirin-containing regimen is prescribed.

Drug Therapy

- Must be in accordance to FDA approved indications.

Sofosbuvir (Sovaldi™)

RECOMMENDED REGIMENS AND TREATMENT DURATION FOR SOFOSBUVIR COMBINATION THERAPY IN HCV[i,ii,iii,iv,v,vi]

HCV Genotype and Comorbidities	Treatment	Duration
Patients with genotype 2 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	12 weeks
Patients with genotype 3 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	24 weeks
Patients with genotype 4 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + peginterferon alfa + ribavirin OR Sofosbuvir + ribavirin	12 weeks 24 weeks

Age Edit: Adult patients age ≥18 years old

Quantity Limit: One 400 mg tablet per day (28 tablets/28 days).

Length of Authorization:

Based on HCV subtype, Patient must be treatment naïve to sofosbuvir.

INITIAL: 8 weeks

REFILLS: Should be reauthorized for additional 8 week period at a time, depending on the treatment plan. The patient must receive refills within one week of completing the previous 28 day supply throughout treatment.

DISCONTINUATION OF DOSING

- It is unlikely that patients with inadequate on-treatment virologic response will achieve a sustained virologic response (SVR) defined as an undetectable HCV RNA 12 weeks post-cessation of therapy, therefore discontinuation of treatment is recommended in these patients.

Treatment Stopping Rules in Any Patient with Inadequate On-Treatment Virologic Response**

HCV RNA	Action
Treatment Week 4: < 2 log reduction in HCV RNA from baseline	Discontinue sofosbuvir, peginterferon alfa and ribavirin
Treatment Week 12: any detectable HCV RNA level	Discontinue peginterferon alfa, ribavirin, and sofosbuvir (if applicable)
Treatment Week 24: any detectable HCV RNA level	Discontinue peginterferon alfa, ribavirin, and sofosbuvir (if applicable)

**** A FDA or AASLD recommendation for the discontinuation of treatment has not been released to date. Prescribers are encouraged to monitor HCV RNA to validate adherence to therapy/efficacy of therapy**

For documented diagnosis of HCV with genotype 2 *[Dual therapy]* Combination with ribavirin – Approval for 12 weeks

- Approve; **OR**
- *Approve* for HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin when starting sofosbuvir for a 12 week duration

For documented diagnosis of HCV with genotype 3 *[Dual therapy]* Combination with ribavirin – Approval for 24 weeks

- Approve; **OR**
- *Approve* for HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin when starting sofosbuvir for a 24 week duration

For diagnosis of HCV with genotype 4 [Dual or Triple therapy] Combination with peginterferon and ribavirin – Approval for 12 or 24 weeks

- Approve; **OR**
- *Approve* for HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin and peginterferon when starting sofosbuvir for a 12 or 24 week duration

ADDITIONAL SOFOSBUVIR INFORMATION TO AID IN THE FINAL DECISION

- Remind all providers that HCV-RNA levels will need to be obtained between treatment weeks 2 and 4 for continuation of treatment
- Approve for 8 weeks of initial therapy to begin with in order to allow time for lab test results to be processed.
- Must have baseline HCV RNA level within 60 days of anticipated treatment start date
- Sofosbuvir combination treatment with ribavirin or peginterferon alfa/ribavirin is contraindicated in women who are pregnant or may become pregnant and men whose female partners are pregnant because of the risks for birth defects and fetal death associated with ribavirin.
- Patient does *not* have severe renal impairment (eGFR <30 mL/min/1.73m^2) or end stage renal disease (ESRD) requiring hemodialysis.
- There is insufficient data to recommend use in patients with HCV genotypes 5 or 6.
- For HIV-1 lab report documenting that patient has HIV-1, patient should be virologically suppressed or provider should provide additional rationale for treatment initiation.

Sofosbuvir/Ledipasvir (Harvoni®)

RECOMMENDED TREATMENT DURATION FOR SOFOSBUVIR/LEDIPASVIR COMBINATION THERAPY IN HCV

HCV Genotype and Comorbidities	Treatment	Duration
Treatment naive patients with genotype 1 HCV with or without cirrhosis	sofosbuvir + ledipasvir	12 weeks*
Treatment experienced patients with genotype 1 HCV without cirrhosis	sofosbuvir + ledipasvir	12 weeks
Treatment experienced patients with genotype 1 HCV with cirrhosis	sofosbuvir + ledipasvir	24 weeks

*8 weeks of treatment can be considered in treatment naive patients without cirrhosis who have pretreatment HCV RNA levels less than 6 million IU/mL.

**Treatment experienced patients include patients who have failed treatment with either peginterferon alpha + ribavirin .

Age Edit: Adult patients age ≥18 years old

Quantity Limit: One 90 mg/400 mg tablet per day (28 tablets/28 days).

Length of Authorization:

Based on treatment experience and cirrhosis, Patient must be treatment naïve to sofosbuvir and ledipasvir

INITIAL: 8 weeks

REFILLS: Should be reauthorized for additional 8 week period at a time, depending on the treatment plan. The patient must receive refills within one week of completing the previous 28 day supply throughout treatment.

DISCONTINUATION OF DOSING

- It is unlikely that patients with inadequate on-treatment virologic response will achieve a sustained virologic response (SVR) defined as an undetectable HCV RNA 12 weeks post-cessation of therapy, therefore discontinuation of treatment is recommended in these patients.

Treatment Stopping Rules in Any Patient with Inadequate On-Treatment Virologic Response**

HCV RNA	Action
Treatment Week 4: < 2 log reduction in HCV RNA from baseline	Discontinue sofosbuvir/ledipasvir
Treatment Week 12: any detectable HCV RNA level	Discontinue sofosbuvir/ledipasvir
Treatment Week 24: any detectable HCV RNA level	Discontinue sofosbuvir/ledipasvir

**** A FDA or AASLD recommendation for the discontinuation of treatment has not been released to date. Prescribers are encouraged to monitor HCV RNA to validate adherence to therapy/efficacy of therapy**

ADDITIONAL SOFOSBUVIR/LEDIPASVIR INFORMATION TO AID IN THE FINAL DECISION

- Remind all providers that HCV-RNA levels will need to be obtained between treatment week 2 and 4 for continuation of treatment
- Approve for 8 weeks of initial therapy to begin with in order to allow time for lab test results to be processed.
- Must have baseline HCV RNA level within 60 days of anticipated treatment start date
- The concomitant use of sofosbuvir/ledipasvir and P-gp inducers (e.g., rifampin, St. John's wort) may significantly decrease ledipasvir and sofosbuvir plasma concentrations and may reduce the therapeutic effect. Therefore, the use of sofosbuvir/ledipasvir with P-gp inducers (e.g., rifampin or St. John's wort) is not recommended.
- Patient does *not* have severe renal impairment (eGFR <30 mL/min/1.73m^2) or end stage renal disease (ESRD) requiring hemodialysis.
- There is insufficient data to recommend use in patients with HCV genotypes other than genotype 1.
- For HIV-1 lab report documenting that patient has HIV-1 patient should be virologically suppressed or provider should provide additional rationale for treatment initiation.

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[i] Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.

[ii] FDA Antiviral Drugs Advisory Committee Meeting, October 25, 2013; Background Package for NDA 204671 sofosbuvir (GS-7977).

[iii] Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.

[iv] Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. N Engl J Med. 2013; 368:1878-87. doi: 10.1056/NEJMoa1214853. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1214853. Accessed January 2, 2014.

[v] Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med. 2013;368:1867-77. doi: 10.1056/NEJMoa1214854. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1214854. Accessed January 2, 2014.

[vi][vi] American Association for the Study of Liver Diseases Infectious Diseases Society of America: Recommendations for testing, managing and treating hepatitis C. Available at: http://www.hcvguidelines.org/. Accessed February 18, 2014.

Sofosbuvir (Sovaldi™) and Simeprevir (Olysio™)[vi,vi]

- **Any request for this therapy will be reviewed on a case-by-case basis by DHMH.**

Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir (Viekira Pak™)

RECOMMENDED TREATMENT DURATION FOR Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir COMBINATION THERAPY IN HCV

HCV Genotype and Comorbidities	Treatment*	Duration
Genotype 1a, without cirrhosis	Viekira Pak™ + ribavirin	12 weeks
Genotype 1a, with cirrhosis	Viekira Pak™ + ribavirin	24 weeks
Genotype 1b, without cirrhosis	Viekira Pak™	12 weeks
Genotype 1b, with cirrhosis	Viekira Pak™ + ribavirin	12 weeks

*Follow genotype 1a dosing recommendations in patients with an unknown genotype 1 subtype or with mixed genotype 1 infection.

Patients with HCV/HIV-1 co-infection: Follow the dosage recommendations in the table above.

Age Edit: Adult patients age ≥18 years old

Quantity Limit: Two ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg tablet per day (56 tablets/28 days) + two dasabuvir 250 mg tablets per day (56 tablets/ 28 days). Note that product is packaged in a monthly carton which contains a total of 28 days of therapy.

Length of Authorization:

Based on genotype, sub-genotype and presence of cirrhosis.

INITIAL: 8 weeks

REFILLS: Should be reauthorized for additional 4 to 8 week period, depending on the treatment plan. The patient must receive refills within one week of completing the previous 28 day supply throughout treatment.

DISCONTINUATION OF DOSING

- It is unlikely that patients with inadequate on-treatment virologic response will achieve a sustained virologic response (SVR) defined as an undetectable HCV RNA 12 weeks post-cessation of therapy, therefore discontinuation of treatment is recommended in these patients.

Treatment Stopping Rules in Any Patient with Inadequate On-Treatment Virologic Response**

HCV RNA	Action
Treatment Week 4: < 2 log reduction in HCV RNA from baseline	Discontinue Viekira Pak™ + ribavirin
Treatment Week 12: any detectable HCV RNA level	Discontinue Viekira Pak™ + ribavirin
Treatment Week 24: any detectable HCV RNA level	Discontinue Viekira Pak™ + ribavirin

**** A FDA or AASLD recommendation for the discontinuation of treatment has not been released to date. Prescribers are encouraged to monitor HCV RNA to validate adherence to therapy/efficacy of therapy**

ADDITIONAL OMBITASVIR/PARITAPREVIR/RITONAVIR/DASABUVIR INFORMATION TO AID IN THE FINAL DECISION

- Remind all providers that HCV-RNA levels will need to be obtained between treatment weeks 2 and 4 for continuation of treatment
- Approve for 8 weeks of initial therapy to begin with in order to allow time for lab test results to be processed.
- Must have baseline HCV RNA level within 60 days of anticipated treatment start date
- Patient is not receiving concomitant therapy with a hepatitis protease inhibitor, HCV polymerase inhibitor or NS5A inhibitor (e.g. boceprevir, simeprevir, ledipasvir or sofosbuvir).
- Viekira Pak™ combination treatment with ribavirin is contraindicated in women who are pregnant or may become pregnant and men whose female partners are pregnant because of the risks for birth defects and fetal death associated with ribavirin.
- Viekira Pak™ is contraindicated in patients with severe hepatic impairment/Child-Pugh C secondary to risk of potential toxicity. Viekira Pak™ is not recommended in patients with moderate hepatic impairment/Child-Pugh B.
- The concomitant use of Viekira Pak™ is contraindicated with medications that are highly dependent on CYP3A for clearance (e.g. alfuzosin, carbamazepine, phenytoin, phenobarbital, gemfibrozil, rifampin, ergot derivatives, ethinyl estradiol containing products, St. John's wort, lovastatin, simvastatin, pimozide, efavirenz, sildenafil when dosed for PAH, triazolam and oral forms of midazolam)
- Viekira Pak™ is contraindicated in patients with known hypersensitivity to ritonavir
- Patient does *not* have end stage renal disease (ESRD) requiring hemodialysis.
- There is insufficient data to recommend use in patients with HCV genotypes other than genotype 1.
- Patients co-infected with HIV and treated with Viekira Pak™ should also be on suppressive antiretroviral therapy for HIV to reduce the risk of HIV protease inhibitor drug resistance, as Viekira Pak™ contains ritonavir.

Retreatment Guidelines

Degree of hepatic damage/treatment experience	Treatment	Duration of Total Therapy
Recommended Treatment genotype 1a		
Patients **(previous PEG-IFN and RBV))** who do NOT have cirrhosis	Ledipasvir/sofosbuvir OR Paritaprevir/ritonavir/ombitasvir + Dasabuvir + Ribavirin	12 weeks
Patients **(previous PEG-IFN and RBV))** who have compensated cirrhosis	Ledipasvir/sofosbuvir OR Ledipasvir/sofosbuvir + ribavirin OR Paritaprevir/ritonavir/ombitasvir + Dasabuvir + Ribavirin	24 weeks 12 weeks 24 weeks
Recommended treatment genotype 1b		
Patients **(PEG-IFN and RBV))** who do NOT have cirrhosis	Ledipasvir/sofosbuvir OR Paritaprevir/ritonavir/ombitasvir + Dasabuvir	12 weeks
Patients **(previous PEG-IFN and RBV))** who have compensated cirrhosis	Ledipasvir/sofosbuvir OR Ledipasvir/sofosbuvir + ribavirin OR Paritaprevir/ritonavir/ombitasvir + Dasabuvir + Ribavirin	24 weeks 12 weeks 12 weeks
Recommended Treatment genotype 2		
Patients with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	12 weeks (patients with cirrhosis may benefit from an extension to 16 weeks of treatment)
Alternative Regimen genotype 2		
Patients **(interferon eligible)** with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + peginterferon alfa + ribavirin	12 weeks
Recommended Treatment genotype 3		

Patients with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	24 weeks
Alternative Regimen genotype 3		
Patients **(interferon eligible)** with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + peginterferon alfa + ribavirin	12 weeks
Recommended treatment genotype 4		
Patients **(interferon eligible)** with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + peginterferon alfa + ribavirin	12 weeks
Alternative Regimen genotype 4		
Patients with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	24 weeks
NOT RECOMMENDED (ALL GENOTYPES)		
Telaprevir, boceprevir, or any monotherapy with any agent		

Note: All requests for retreatment for patients with prior protease inhibitor experience should be sent to DHMH for approval.